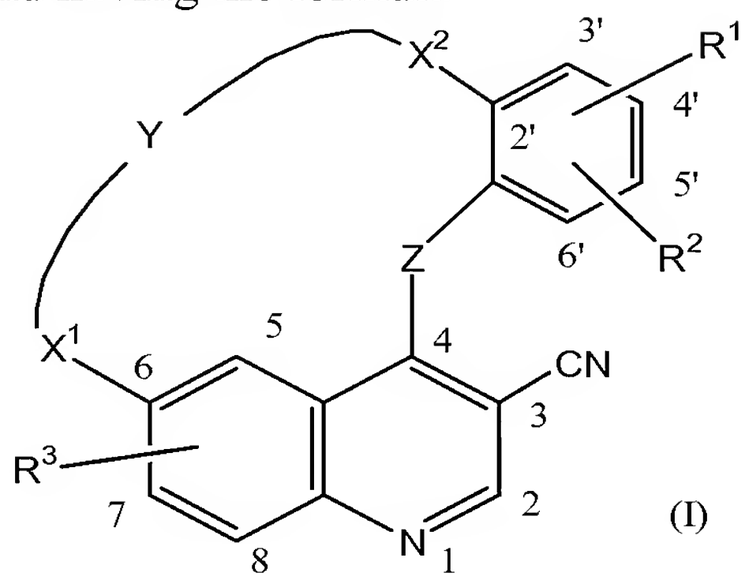
Listing of Claims

1. (Original) A compound having the formula



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

Z represents O, NH or S;

Y represents -C_{3-9}alkyl-, -C_{3-9}alkenyl-, -C_{1-5}alkyl-oxy-C_{1-5}alkyl-, -C_{1-5}alkyl-NR^{12}-C_{1-5}alkyl-, -C_{1-5}alkyl-NR^{13}-CO-C_{1-5}alkyl-, -C_{1-5}alkyl-CO-NR^{14}-C_{1-5}alkyl-, -C_{1-6}alkyl-CO-NH-, -C_{1-6}alkyl-NH-CO-, -CO-NH-C_{1-6}alkyl-, -NH-CO-C_{1-6}alkyl-, -CO-C_{1-7}alkyl-, -C_{1-7}alkyl-CO-, C_{1-6}alkyl-CO-C_{1-6}alkyl, -C_{1-2}alkyl-NH-CO-CH_2R^{15}-NH-;

X^1 represents a direct bond, O, -O-C_{1-2}alkyl-, CO, -CO- C_{1-2}alkyl-, NR^{10}, -NR^{10}-C_{1-2}alkyl-, NR^{16}-CO-, NR^{16}-CO-C_{1-2}alkyl, -O-N=CH- or C_{1-2}alkyl;

X^2 represents a direct bond, O, -O-C_{1-2}alkyl-, CO, -CO- C_{1-2}alkyl-, NR^{11}, NR^{11}-C_{1-2}alkyl-, NR^{17}-CO-, NR^{17}-CO-C_{1-2}alkyl, Het^{20}-C_{1-2}alkyl, -O-N=CH- or C_{1-2}alkyl;

R^1 represents hydrogen, cyano, halo, hydroxy, formyl, C_{1-6}alkoxy-, C_{1-6}alkyl-,
C_{1-6}alkoxy- substituted with halo,
C_{1-4}alkyl substituted with one or where possible two or more substituents selected from hydroxy or halo;

R^2 represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, Het^{16}-carbonyl-, C_{1-4}alkyloxycarbonyl-, C_{1-4}alkylcarbonyl-, aminocarbonyl-, mono-or di(C_{1-4}alkyl)aminocarbonyl-, Het^1, formyl, C_{1-4}alkyl-, C_{2-6}alkynyl-, C_{3-6}cycloalkyl-, C_{3-6}cycloalkyloxy-, C_{1-6}alkoxy-, Ar^5, Ar^1-oxy-, dihydroxyborane ,
C_{1-6}alkoxy- substituted with halo,
C_{1-4}alkyl substituted with one or where possible two or more substituents selected from halo, hydroxy or NR^4R^5,

C_{1-4}alkylcarbonyl- wherein said C_{1-4}alkyl is optionally substituted with one or where possible two or more substituents selected from hydroxy or C_{1-4}alkyl-oxy-;

R^3 represents hydrogen, hydroxy, Ar^3-oxy, Ar^4-C_{1-4}alkyloxy-, C_{1-4}alkyloxy-, C_{2-4}alkenyloxy- optionally substituted with Het^{12} or R^3 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy-, hydroxy, halo, Het^2-, -NR^6R^7, -carbonyl- NR^8R^9 or Het^3-carbonyl-;

R^4 and R^5 are each independently selected from hydrogen or C_{1-4}alkyl;

R^6 and R^7 are each independently selected from hydrogen, C_{1-4}alkyl, Het^8, aminosulfonyl-, mono- or di (C_{1-4}alkyl)-aminosulfonyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxycarbonyl-C_{1-4}alkyl-, C_{3-6}cycloalkyl, Het^9-carbonyl-C_{1-4}alkyl-, Het^{10}-carbonyl-, polyhydroxy-C_{1-4}alkyl-, Het^{11}-C_{1-4}alkyl- or Ar^2-C_{1-4}alkyl-;

R^8 and R^9 are each independently selected from hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, Het^4, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or polyhydroxy-C_{1-4}alkyl-;

R^{10} represents hydrogen, C_{1-4}alkyl, Het^5, Het^6-C_{1-4}alkyl-, C_{2-4}alkenylcarbonyl- optionally substituted with Het^7-C_{1-4}alkylaminocarbonyl-, C_{2-4}alkenylsulfonyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;

R^{11} represents hydrogen, C_{1-4}alkyl, C_{1-4}alkyl-oxy-carbonyl-, Het^{17}, Het^{18}-C_{1-4}alkyl-, C_{2-4}alkenylcarbonyl- optionally substituted with Het^{19}-C_{1-4}alkylaminocarbonyl-, C_{2-4}alkenylsulfonyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;

R^{12} represents hydrogen, C_{1-4}alkyl, Het^{13}, Het^{14}-C_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;

R^{13} and R^{14} are each independently selected from hydrogen, C_{1-4}alkyl, Het^{15}-C_{1-4}alkyl- or C_{1-4}alkyloxyC_{1-4}alkyl-;

R^{15} represents hydrogen or C_{1-4}alkyl optionally substituted with phenyl, indolyl, methylsulfide, hydroxy, thiol, hydroxyphenyl, aminocarbonyl, hydroxycarbonyl, amine, imidazoyl or guanidino;

R^{16} and R^{17} are each independently selected from hydrogen, C_{1-4}alkyl, Het^{21}-C_{1-4}alkyl or C_{1-4}alkyloxyC_{1-4}alkyl;

Het^1 represents a heterocycle selected from piperidinyl, morpholinyl, piperazinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^1 is optionally substituted

amino, C_{1-4}alkyl, hydroxy-C_{1-4}alkyl-, phenyl, phenyl-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl- mono- or di(C_{1-4}alkyl)amino- or amino-carbonyl-;

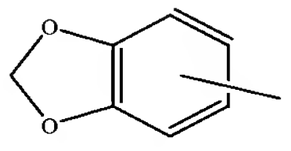
Het^2 represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het^2 is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-oxy-C_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino-, mono- or di(C_{1-4}alkyl)amino-C_{1-4}alkyl-, aminoC_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino-sulfonyl-, aminosulfonyl-;

Het^3, Het^4 and Het^8 each independently represent a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^3, Het^4 or Het^8 is optionally substituted with one or where possible two or more substituents selected from hydroxy-, amino-, C_{1-4}alkyl-, C_{3-6}cycloalkyl-C_{1-4}alkyl-, aminosulfonyl-, mono- or di(C_{1-4}alkyl)aminosulfonyl or amino-C_{1-4}alkyl-;

Het^5 represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^5 optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^6 and Het^7 each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het^6 and Het^7 are optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^9 and Het^{10} each independently represent a heterocycle selected from furanyl, piperidinyl, morpholinyl, piperazinyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^9 or Het^{10} is optionally substituted C_{1-4}alkyl, C_{3-6}cycloalkyl-C_{1-4}alkyl- or amino-C_{1-4}alkyl-;

Het^{11} represents a heterocycle selected from indolyl or  ;

Het^{12} represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het^{12} is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-,

hydroxy-C_{1-4}alkyl-oxy-C_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino- or mono- or di(C_{1-4}alkyl)amino-C_{1-4}alkyl-;

Het^{13} represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^{13} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}allkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{14} represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het^{14} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}allkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{15} and Het^{21} each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said heterocycles are optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{16} represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl, 1,3,2-dioxaborolane or piperidinyl wherein said heterocycle is optionally substituted with one or more substituents selected from C_{1-4}alkyl; and

Het^{17} represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^{17} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{18} and Het^{19} each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het^{18} and Het^{19} are optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{20} represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, imidazolyl or pyrazolidinyl wherein said Het^{20} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-; and

Ar^1, Ar^2, Ar^3, Ar^4 and Ar^5 each independently represent phenyl optionally substituted with cyano, C_{1-4}alkylsulfonyl-, C_{1-4}alkylsulfonylamino-, aminosulfonylamino-, hydroxy-C_{1-4}alkyl, aminosulfonyl-, hydroxy-, C_{1-4}alkyloxy- or C_{1-4}alkyl.

2. (Currently Amended) A compound according to claim 1 wherein;

~~Another group of compounds consists of those compounds of formula (I) wherein one or more of the following restrictions apply:~~

Z represents NH;

Y represents -C_{3-9}alkyl-, -C_{2-9}alkenyl-, -C_{1-5}alkyl-oxy-C_{1-5}alkyl-, -C_{1-5}alkyl-NR^{12}-C_{1-5}alkyl-, -C_{1-5}alkyl-NR^{13}-CO-C_{1-5}alkyl-, -C_{1-6}alkyl-NH-CO-, -CO-C_{1-7}alkyl-, -C_{1-7}alkyl-CO- or C_{1-6}alkyl-CO-C_{1-6}alkyl;

X^1 represents O, -O-C_{1-2}alkyl-, -O-N=CH-, NR^{16}-CO, -NR^{16}-CO-C_{1-2}alkyl-, NR^{10} or -NR^{10}-C_{1-2}alkyl-; in a particular embodiment X^1 represents –O-, –O-CH_2-, NR^{10} or -NR^{10}-C_{1-2}alkyl-;

X^2 represents a direct bond, O, -O-C_{1-2}alkyl-, -O-N=CH-, Het^{20}-C_{1-2}alkyl, C_{1-2}alkyl, NR^{17}-CO, -NR^{17}-CO-C_{1-2}alkyl-, NR^{11} or NR^{11}-C_{1-2}alkyl-; in a particular embodiment X^2 represents a direct bond, –O-N=CH-, -NR^{11}-C_{1-2}alkyl-, -NR^{11}-CH_2-, Het^{20}-C_{1-2}alkyl, NR^{17}-CO, -NR^{17}-CO-C_{1-2}alkyl- -C_{1-2}alkyl-, -O-C_{1-2}alkyl, –O- or –O-CH_2-;

R^1 represents hydrogen, cyano, halo or hydroxy, preferably halo;

R^2 represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, C_{1-4}alkyloxycarbonyl-, Het^{16}-carbonyl-, C_{2-6}alkynyl-, Ar^5 or Het^1;

In a further embodiment R^2 represents hydrogen, cyano, halo, hydroxy, C_{2-6}alkynyl- or Het^1;

R^3 represents hydrogen, hydroxy, C_{1-4}alkyloxy-, Ar^4-C_{1-4}alkyloxy or R^3 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy- or Het^2-;

R^{10} represents hydrogen, C_{1-4}alkyl- or C_{1-4}alkyl-oxy-carbonyl-;

R^{11} represents hydrogen, C_{1-4}alkyl- or C_{1-4}alkyl-oxy-carbonyl-;

R^{12} represents Het^{14}-C_{1-4}alkyl, in particular morpholinyl-C_{1-4}alkyl;

R^{16} represents hydrogen, C_{1-4}alkyl-, Het^{21}-C_{1-4}alkyl or C_{1-4}alkyl-oxy-C_{1-4}alkyl; in particular R^{16} represents hydrogen or C_{1-4}alkyl;

R^{17} represents hydrogen, C_{1-4}alkyl-, Het^{21}-C_{1-4}alkyl or C_{1-4}alkyl-oxy-C_{1-4}alkyl; in particular R^{16} represents hydrogen or C_{1-4}alkyl;

Het^1 represents thiazolyl optionally substituted amino, C_{1-4}alkyl, hydroxy-C_{1-4}alkyl-, phenyl, phenyl-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl- mono- or di(C_{1-4}alkyl)amino- or amino-carbonyl-;

Het^2 represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^2 is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl-;

~~In a further embodiment Het^2 represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C_{1-4}alkyl-, preferably methyl;~~

Het^{14} represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^{14} is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl-;
Het^{16} represents a heterocycle selected from piperidinyl, morpholinyl or pyrrolidinyl;
Het^{20} represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl or piperidinyl;
Het^{21} represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^{21} is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl-;
Ar^4 represents phenyl optionally substituted with cyano, hydroxy-, C_{1-4}alkyloxy or C_{1-4}alkyl;
Ar^5 represents phenyl optionally substituted with cyano, hydroxy, C_{1-4}alkyloxy or C_{1-4}alkyl.

3. (Currently Amended) A compound according to claim 1 wherein;
Z represents NH;
Y represents $-C_{3-9}$alkyl-, $-C_{1-5}$alkyl-NR^{12}-C_{1-5}alkyl-, $-C_{1-5}$alkyl-NR^{13}-CO-C_{1-5}alkyl-, $-C_{1-6}$alkyl-NH-CO- or -CO-NH $-C_{1-6}$alkyl-;
X^1 represents a direct bond, NR^{10}, $-NR^{10}$-C_{1-2}alkyl-, $-NR^{10}$-CH_2-, $-C_{1-2}$alkyl-, -O-C_{1-2}alkyl, -O- or –O-CH_2-;
X^2 represents a-O-, NR^{11}, NR^{17}-CO, NR^{17}-CO-C_{1-2}alkyl or Het^{20}-C_{1-2}alkyl;
R^1 represents hydrogen or halo;
R^2 represents hydrogen, cyano, halo, hydroxycarbonyl-, C_{1-4}alkyloxycarbonyl-, Het^{16}-carbonyl- or Ar^5;
R^3 represents hydrogen, hydroxy, C_{1-4}alkyloxy-, Ar^4-C_{1-4}alkyloxy or R^3 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy- or Het^2-;
R^{10} represents hydrogen;
R^{11} represents hydrogen, C_{1-4}alkyl- or C_{1-4}alkyl-oxy-carbonyl-;
R^{12} represents Het^{14}-C_{1-4}alkyl, in particular morpholinyl-C_{1-4}alkyl;
R^{13} represents hydrogen;
R^{17} represents hydrogen;
Het^2 represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^2 is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl-;
~~In a further embodiment Het^2 represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C_{1-4}alkyl-, preferably methyl;~~
Het^{14} represents morpholinyl;

Het^{16} represents a heterocycle selected from morpholinyl or pyrrolidinyl;
Het^{20} represents pyrrolidinyl or piperidinyl;
Ar^4 represents phenyl;
Ar^5 represents phenyl optionally substituted with cyano.

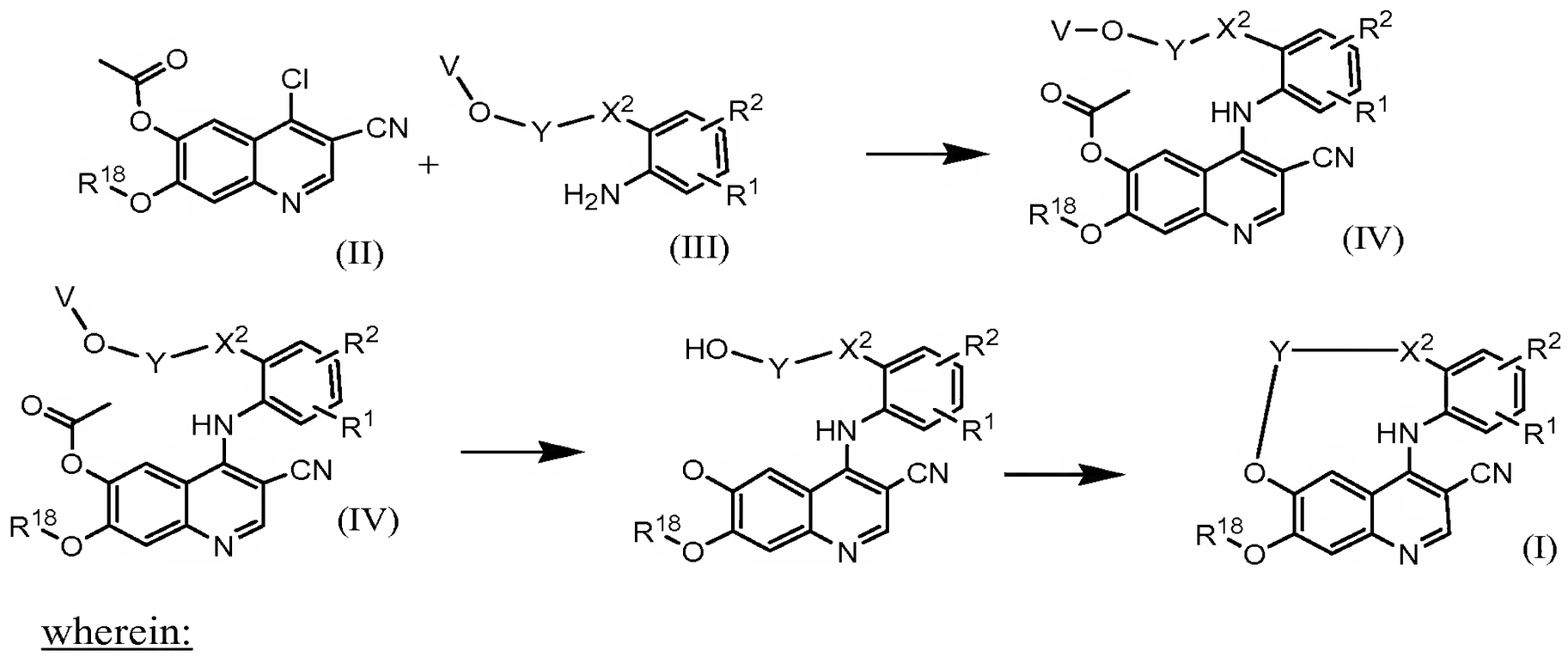
4. (Currently Amended) A compound according to claim 1,~~any one of claims 1 to 3~~ wherein the R^1 substituent is at position 4', the R^2 substituent is at position 5' and the R^3 substituent at position 7 of the structure of formula (I).

5.-7. (Cancelled)

8. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, an effective kinase inhibitory amount of a compound as described in claim 1~~any one of the claims 1 to~~ 4.

9. (Currently Amended) A process for preparing a compound as claimed in claim 1~~claims 1 to 4~~, comprising~~;~~:

a) coupling the known 6-acetoxy-4-chloro-3-cyano- quinolines of formula (II) with the suitable substituted anilines of formula (III) to furnish the intermediates of formula (IV), and deprotecting the intermediates of formula (IV) followed by ring closure under suitable conditions:

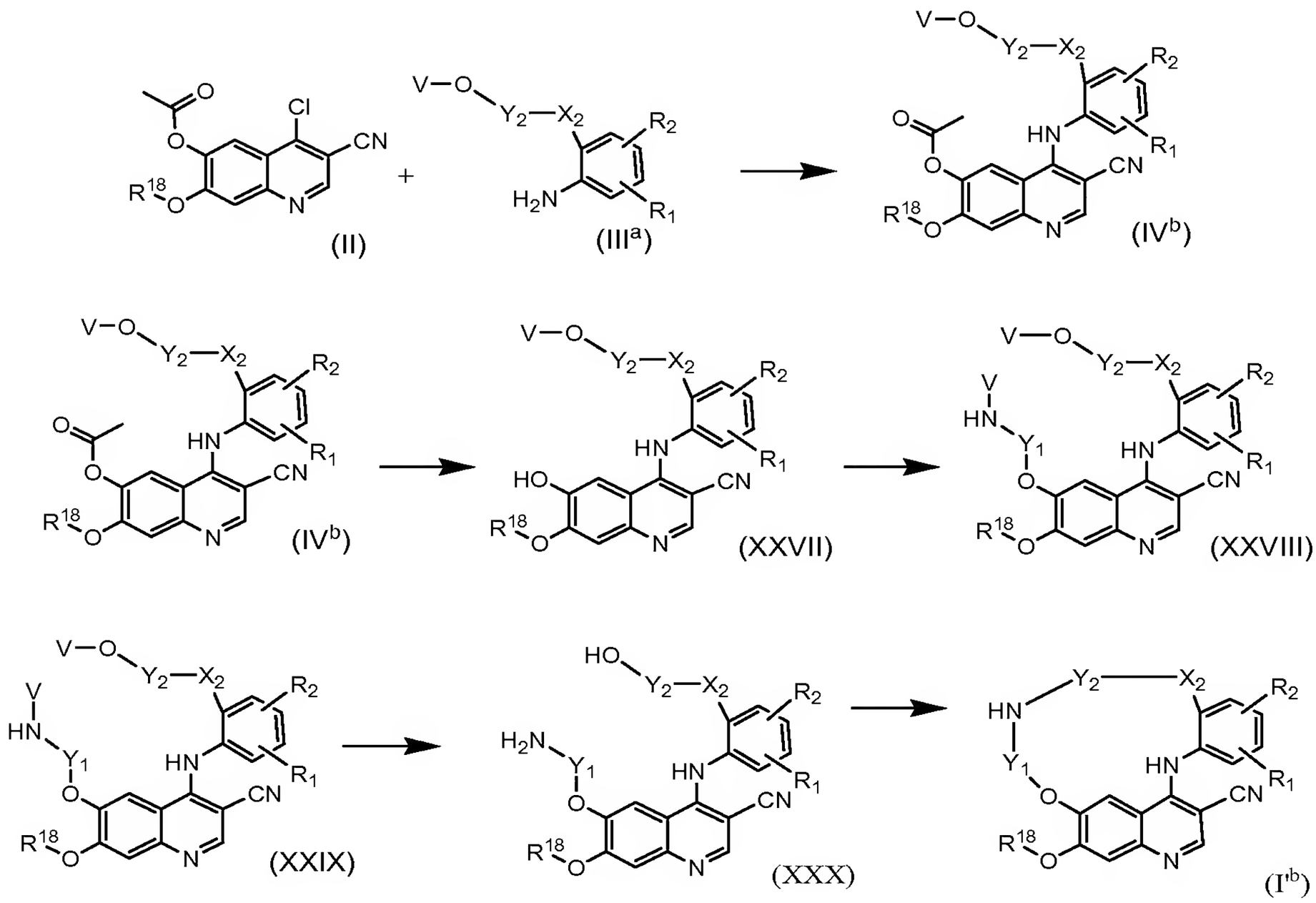


wherein:

V = protective group such as for example methylcarbonyl, t-butyl, methyl, ethyl, benzyl or trialkylsilyl groups,

R^{18} represents Ar^3, Ar^4-C_{1-4}alkyl, C_{1-4}alkyl, C_{2-6}alkenyl optionally substituted with Het^{12} or R^{18} represents C_{1-4}alkyl substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy, hydroxy, halo, Het^2, NR^7R^8, NR^9R^{10}-carbonyl or Het^3-carbonyl, wherein Ar^3, Ar^4, Het^{12}, Het^2, R^7, R^8, R^9, R^{10} and Het^3 are defined as for the compounds of formula (I);

b) deprotection of the intermediates of formula (IV^b) and subsequent formation of the corresponding ether using the appropriate aminated alcohol under standard conditions provides the intermediates of formula (XXVIII). Deprotection followed by ring closure provides the target compounds of formula (I'^b).



wherein:

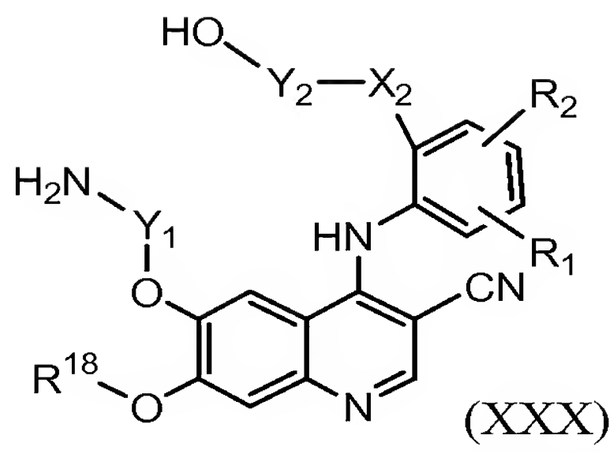
V = protective group such as for example, methylcarbonyl, t-butyl, methyl, ethyl, benzyl or trialkylsilyl groups, or in case of solid phase chemistry the resin to which the remainder of the molecule is attached,

R^{18}represents Ar^3, Ar^4-C_{1-4}alkyl, C_{1-4}alkyl, C_{2-6}alkenyl optionally substituted with Het^{12} or R^{18} represents C_{1-4}alkyl substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy, hydroxy, halo, Het^2, NR^6R^7, NR^8R^9-carbonyl or Het^3-carbonyl, wherein Ar^3, Ar^4, Het^{12}, Het^2, R^6, R^7, R^8, R^9 and Het^3 are defined as for the compounds of formula (I)

Y_1 and Y_2 each independently represent a C_{1-5}alkyl, CO-C_{1-5}alkyl or CO-CH_2R^{16}-NH- ,

10. (Currently Amended) A method of treating a cell proliferative disorder, the method comprising administering to an animal in need of such treatment a therapeutically effective amount of a compound as claimed in claim 1~~any one of claims 1 to 4~~.

11. (Currently Amended) ~~An intermediate~~ A compound of formula (XXX)



(XXX)

the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

Y_1 and Y_2 each independently represent C_{1-5}alkyl, CO-C_{1-5}alkyl or CO-CH_2R^{15}-NH-;

X^1 represents a direct bond, O, -O-C_{1-2}alkyl-, CO, -CO- C_{1-2}alkyl-, NR^{10}, -NR^{10}-C_{1-2}alkyl-, -CH_2-, -O-N=CH- or -C_{1-2}alkyl-;

X^2 represents a direct bond, O, -O-C_{1-2}alkyl-, CO, -CO- C_{1-2}alkyl-, NR^{11}, -NR^{11}-C_{1-2}alkyl-, -CH_2-, -O-N=CH- or C_{1-2}alkyl;

R^1 represents hydrogen, cyano, halo, hydroxy, formyl, C_{1-6}alkoxy-, C_{1-6}alkyl-, C_{1-6}alkoxy- substituted with halo, C_{1-4}alkyl substituted with one or where possible two or more substituents selected from hydroxy or halo; and

R^2 represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, Het^{16}-carbonyl-, C_{1-4}alkyloxycarbonyl-, C_{1-4}alkylcarbonyl-, aminocarbonyl-, mono-or di(C_{1-4}alkyl)aminocarbonyl-, Het^1, formyl, C_{1-4}alkyl-, C_{2-6}alkynyl-, C_{3-6}cycloalkyl-, C_{3-6}cycloalkyloxy-, C_{1-6}alkoxy-, Ar^5, Ar^1-oxy-, dihydroxyborane , C_{1-6}alkoxy- substituted with halo, C_{1-4}alkyl substituted with one or where possible two or more substituents selected from halo, hydroxy or NR^4R^5, C_{1-4}alkylcarbonyl- wherein said C_{1-4}alkyl is optionally substituted with one or where possible two or more substituents selected from hydroxy or C_{1-4}alkyl-oxy-;

R^4 and R^5 are each independently selected from hydrogen or C_{1-4}alkyl;

R^6 and R^7 are each independently selected from hydrogen, C_{1-4}alkyl, Het^8, aminosulfonyl-, mono- or di (C_{1-4}alkyl)-aminosulfonyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxycarbonyl-C_{1-4}alkyl-, C_{3-6}cycloalkyl, Het^9-carbonyl-C_{1-4}alkyl-, Het^{10}-carbonyl-, polyhydroxy-C_{1-4}alkyl-, Het^{11}-C_{1-4}alkyl- or Ar^2-C_{1-4}alkyl-;

R^8 and R^9 are each independently selected from hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, Het^4, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or polyhydroxy-C_{1-4}alkyl-;

R^{10} represents hydrogen, C_{1-4}alkyl, C_{1-4}alkyl-oxy-carbonyl-, Het^{17}, Het^{18}-C_{1-4}alkyl-, C_{2-4}alkenylcarbonyl- optionally substituted with Het^{19}-C_{1-4}alkylaminocarbonyl-,

C_{2-4}alkenylsulfonyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;

R^{11} represents hydrogen, C_{1-4}alkyl, Het^{13}, Het^{14}-C_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;

R^{15} represents hydrogen or C_{1-4}alkyl optionally substituted with phenyl, indolyl, methylsulfide, hydroxy, thiol, hydroxyphenyl, aminocarbonyl, hydroxycarbonyl, amine, imidazoyl or guanidino;

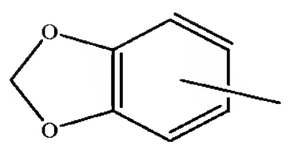
R^{18} represents Ar^3, Ar^4-C_{1-4}alkyl, C_{1-4}alkyl, C_{2-6}alkenyl optionally substituted with Het^{12} or R^{18} represents C_{1-4}alkyl substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy, hydroxy, halo, Het^2, NR^6R^7, NR^8R^9-carbonyl or Het^3-carbonyl;

Het^1 represents a heterocycle selected from piperidinyl, morpholinyl, piperazinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^1 is optionally substituted amino, C_{1-4}alkyl, hydroxy-C_{1-4}alkyl-, phenyl, phenyl-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl- mono- or di(C_{1-4}alkyl)amino- or amino-carbonyl-;

Het^2 represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het^2 is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-oxy-C_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino-, mono- or di(C_{1-4}alkyl)amino-C_{1-4}alkyl-, aminoC_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino-sulfonyl-, aminosulfonyl-;

Het^3, Het^4 and Het^8 each independently represent a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^3, Het^4 or Het^8 is optionally substituted with one or where possible two or more substituents selected from hydroxy-, amino-, C_{1-4}alkyl-, C_{3-6}cycloalkyl-C_{1-4}alkyl-, aminosulfonyl-, mono- or di(C_{1-4}alkyl)aminosulfonyl or amino-C_{1-4}alkyl-;

Het^9 and Het^{10} each independently represent a heterocycle selected from furanyl, piperidinyl, morpholinyl, piperazinyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^9 or Het^{10} is optionally substituted C_{1-4}alkyl, C_{3-6}cycloalkyl-C_{1-4}alkyl- or amino-C_{1-4}alkyl-;

Het^{11} represents a heterocycle selected from indolyl or  ;

Het^{12} represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het^{12} is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-oxy-C_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino- or mono- or di(C_{1-4}alkyl)amino-C_{1-4}alkyl-;

Het^{13} represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^{13} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}allkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{14} represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het^{14} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}allkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{16} represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl, 1,3,2-dioxaborolane or piperidinyl wherein said heterocycle is optionally substituted with one or more substituents selected from C_{1-4}alkyl; and

Het^{17} represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^{17} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{18} and Het^{19} each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein Het^{18} and Het^{19} are optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Ar^1, Ar^3, Ar^4 and Ar^5 each independently represent phenyl optionally substituted with cyano, C_{1-4}alkylsulfonyl-, C_{1-4}alkylsulfonylamino-, aminosulfonylamino-, hydroxy-C_{1-4}alkyl, aminosulfonyl-, hydroxy-, C_{1-4}alkyloxy- or C_{1-4}alkyl.

12. (Cancelled).